HLA-DQA1 gene

major histocompatibility complex, class II, DQ alpha 1

Normal Function

The *HLA-DQA1* gene provides instructions for making a protein that plays a critical role in the immune system. The *HLA-DQA1* gene is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria.

The HLA complex is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. The *HLA-DQA1* gene belongs to a group of MHC genes called MHC class II. MHC class II genes provide instructions for making proteins that are present on the surface of certain immune system cells. These proteins attach to protein fragments (peptides) outside the cell. MHC class II proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it triggers a response to attack the invading viruses or bacteria.

The protein produced from the *HLA-DQA1* gene attaches (binds) to the protein produced from another MHC class II gene, *HLA-DQB1*. Together, they form a functional protein complex called an antigen-binding DQαβ heterodimer. This complex displays foreign peptides to the immune system to trigger the body's immune response.

Each MHC class II gene has many possible variations, allowing the immune system to react to a wide range of foreign invaders. Researchers have identified hundreds of different versions (alleles) of the *HLA-DQA1* gene, each of which is given a particular number (such as *HLA-DQA1*05:01*).

Health Conditions Related to Genetic Changes

autoimmune Addison disease

celiac disease

At least two specific combinations of HLA gene variants (HLA haplotypes) have been found to increase the risk of developing celiac disease, a disorder in which inflammation damages the intestinal tract and other organs and tissues. One of these haplotypes, known as DQ2, is composed of the protein produced from *HLA-DQA1* gene variants known as *HLA-DQA1*05:01* or *HLA-DQA1*05:05* bound to the protein produced from *HLA-DQB1* gene variants known as *HLA-DQB1*02:01*

or *HLA-DQB1*02:02*. The other haplotype, known as DQ8, is composed of the protein produced from *HLA-DQA1* gene variants known as *HLA-DQA1*03:01* or *HLA-DQA1*03:02* bound to the protein produced from the *HLA-DQB1* gene variant known as *HLA-DQB1*03:02*.

The DQ2 and DQ8 haplotypes, which may occur separately or together, seem to increase the risk of an inappropriate immune response to the protein gluten, which is found in wheat, rye, and barley. This immune system malfunction results in the damage to the body's organs and tissues that occurs in celiac disease. However, the DQ2 and DQ8 haplotypes are also found in 30 percent of the general population, and only 3 percent of individuals with these haplotypes develop celiac disease.

idiopathic inflammatory myopathy

juvenile idiopathic arthritis

narcolepsy

type 1 diabetes

Combinations of variations in the *HLA-DQA1* gene and other HLA genes affect the risk of type 1 diabetes. Type 1 diabetes is characterized by high blood sugar levels resulting from a shortage of the hormone insulin and is caused by autoimmune damage to insulin-producing cells in the pancreas.

Type 1 diabetes risk is most increased by two HLA haplotypes involving variations of the *HLA-DQA1* and *HLA-DQB1* genes and another HLA gene called *HLA-DRB1*. One haplotype, written as *DRB1*03:01-DQA1*05:01-DQB1*02*, is called DR3. The other haplotype, written as *DRB1*04:01/02/04/05/08-DQA1*03:01-DQB1*02*, is called DR4. People at highest risk of developing type 1 diabetes have one copy of the DR3 haplotype and one copy of the DR4 haplotype in each cell. Other HLA haplotypes only mildly increase the risk of type 1 diabetes, while some haplotypes seem to protect against developing this condition. Variations in other genes and environmental factors are also thought to affect the risk of this complex disorder.

autoimmune disorders

Certain normal variations of the *HLA-DQA1* gene have been associated with increased risk of autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. It is unclear how different versions of the *HLA-DQA1* gene influence the risk of developing autoimmune disorders. These conditions are thought to result from a combination of multiple environmental and genetic factors. Changes in other HLA and non-HLA genes, some of which remain unknown, also likely contribute to the risk of developing these complex conditions.

other disorders

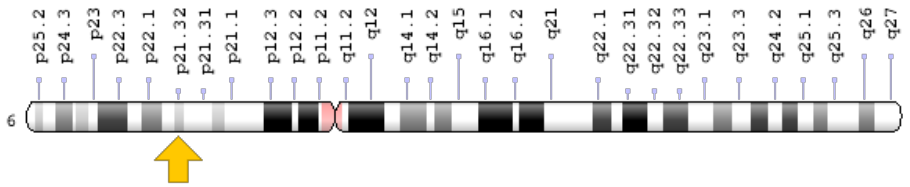
Normal variations in the *HLA-DQA1* gene can affect the body's ability to recognize and react to foreign invaders (pathogens). For example, variations of this gene have been shown to increase or decrease a person's chance of getting infections such as hepatitis B and leprosy or may affect the severity of illness if infection occurs.

A particular variant of the *HLA-DQA1* gene known as *HLA-DQA1*02:01* increases the risk of liver damage in women with advanced breast cancer treated with a drug called lapatinib. Researchers suggest that the variant may increase immune system sensitivity to the drug, resulting in inflammation that damages the liver.

Chromosomal Location

Cytogenetic Location: 6p21.32, which is the short (p) arm of chromosome 6 at position 21.32

Molecular Location: base pairs 32,637,403 to 32,654,846 on chromosome 6 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DC-1 alpha chain
- DC-alpha
- DQ-A1
- FLJ27088
- FLJ27328
- GSE
- HLA class II histocompatibility antigen, DQ alpha 1 chain
- HLA class II histocompatibility antigen, DQ alpha 1 chain precursor
- HLA class II histocompatibility antigen, DQ(W3) alpha chain
- HLA-DCA

- HLA-DQA
- leucocyte antigen DQA1
- leukocyte antigen alpha chain
- MGC149527
- MHC class II antigen
- MHC class II DQA1
- MHC class II HLA-D alpha glycoprotein
- MHC class II HLA-DQ-alpha-1
- MHC class II surface glycoprotein
- MHC HLA-DQ alpha

Additional Information & Resources

Educational Resources

- Immunobiology (fifth edition, 2001): The Major Histocompatibility Complex and Its Functions
  https://www.ncbi.nlm.nih.gov/books/NBK27156/
- National Center for Biotechnology Information (2004): The Genetic Landscape of Diabetes
  https://www.ncbi.nlm.nih.gov/books/NBK1667/
- The Merck Manual for Health Professionals: Human Leukocyte Antigen (HLA) System
  http://www.merckmanuals.com/professional/immunology-allergic-disorders/biology-of-the-immune-system/human-leukocyte-antigen-hla-system

GeneReviews

- Celiac Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1727

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28HLA-DQA1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- MAJOR HISTOCOMPATIBILITY COMPLEX, CLASS II, DQ ALPHA-1
  http://omim.org/entry/146880

Research Resources

- Anthony Nolan Research Institute: Nomenclature for Factors of the HLA System
  http://hla.alleles.org/nomenclature/index.html
- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_HLA-DQA1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HLA-DQA1%5Bgene%5D
- HGNC Gene Family: C1-set domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/591
- HGNC Gene Family: Histocompatibility complex
  http://www.genenames.org/cgi-bin/genefamilies/set/588
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4942
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3117
- UniProt
  http://www.uniprot.org/uniprot/P01909

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- GeneReview: Celiac Disease
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